



**THE UNIVERSITY OF CHICAGO**

**Group Art Unit: 1627**

**Attorney**  
**Docket: 01/21362**

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**For: COMBINATORIAL COMPLEX  
CARBOHYDRATE LIBRARIES  
AND METHODS FOR THE  
MANUFACTURE AND USES  
THEREOF**

**Examiner: Epperson, Jon D**

**Commissioner of Patents and Trademarks**  
**Washington, D.C. 20231**

I am presently Professor Emeritus at the Department of Biological Chemistry of the Weizmann Institute of Science. I received my Ph.D. in Biochemistry from the Hebrew University in Jerusalem in 1954 and completed post doctoral work at the Harvard Medical School. During the course of my tenure at the Weizmann Institute of Science, I was head of Department and Faculty dean, I was also a visiting Professor at a number of institutions including the University of California at Berkley, Oxford University, Harvard University. In addition, I was a Fogarty Scholar at the National Institute of Health, in Bethesda, MD.

I am the recipient of national and international awards and honors, including the Israel Prize for Biochemistry and an honorary Doctorate from the University of Paris. I am a member of the Israel Academy of Sciences and Humanities, and of Academia Europea, as well as an honorary member of the American Society for Biochemistry and Molecular biology and of the American Society of Microbiology. I was selected to the advisory committee of the

Consortium for Functional Glycomics established by the National Institutes of Health, Bethesda, MD.

For nearly half a century, my research focused on carbohydrates and carbohydrate binding proteins. I have published more than 450 scientific articles in highly regarded journals many of which are widely cited, and several books including "Complex Carbohydrates" (Addison Wesley, 1975, Japanese translation in 1977) which was the first, and until recently the only, textbook published on the subject.

I have read the Official action issued with respect to the above-identified application and I disagree with the Examiner's comments regarding the synthesis and use of the addressable complex carbohydrate libraries described in the application.

The idea of producing an array of complex carbohydrates on a single flat substrate and the use of glycosyltransferases for *in situ* solid phase synthesis of complex carbohydrate structures was first introduced to me by Dr. Nir Dotan and Dr. Avinoam Dukler, the inventors in this case, on March 1999 at a meeting held at my house in Tel-Aviv, Israel. At that meeting, they suggested that such an array would be extremely useful for the high throughput detection of carbohydrate binding proteins such as lectins, antibodies and enzymes and for establishing the specificity of such proteins.

Since at the time, complex carbohydrate arrays were neither described nor suggested in the art, I was immediately struck by the novelty and originality of their idea and its importance, especially in view of the widespread interest in complex carbohydrate structures both in Academia and in the Biotech industry.

In addition to recognizing the applicability of such novel arrays, I was extremely impressed by the novel synthetic approach described to me by the inventors.

Enzymes of the glycosyltransferase family are ideal for complex carbohydrate synthesis since such enzymes are accurate and efficient in creating the glycosidic bond, they require moderate conditions for synthesis and are highly

diverse enabling synthesis of a wide repertoire of carbohydrate structures. Although numerous glycosyltransferases were available prior to filing of the instant application, only four types -  $\beta$  1,4 galactosyltransferase,  $\alpha$  2,3 and  $\alpha$  2,6 sialyltransferase and  $\alpha$  1,3/4 fucosyltransferase - were routinely used in carbohydrate synthesis.

In addition, although enzymatic synthesis of oligosaccharides in solution or on insoluble carriers (particulates, beads) was previously described in the art, parallel enzymatic synthesis of complex carbohydrate libraries bound in an addressable manner to a single support (e.g., an array) has not been previously described. In fact, publications describing carbohydrate arrays and synthesis approaches suitable for generation of such arrays have appeared only in the last year, again emphasizing the novelty and importance of the support-bound addressable complex carbohydrate libraries of the present invention.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are considered to be true too; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

23 December, 2002

Nathan Sharon

Prof. Nathan Sharon

*Encl.*

CV of Prof. Nathan Sharon

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